AF/1651 IFW

Attorney Docket No.: 5248.210-US PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Charlotte Johansen Confirmation No: 3908

Serial No.: 09/768,803 Group Art Unit: 1651

Filed: January 24, 2001 Examiner: I. Marx

For: Antimicrobial Composition Containing A Haloperoxidase, A Hydrogen Peroxide Source, A Halide Source And An Ammonium Source

CERTIFICATE OF MAILING UNDER 37 CFR 1.8(a)

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I hereby certify that the attached correspondence comprising:

1. Transmitttal of Appeal Brief (in duplicate)
2. Brief on Appeal and a copy of pending claims (in triplicate)

is being deposited with the United States Postal Service as first class mail in an envelope addressed to the address indicated above on June 24, 2004.

Else-Marie Ulderup
(name of person mailing paper)

Else-Marie Ulderup
(signature of person mailing paper)

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TRANSMITTAL OF APPEAL BRIEF

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Transmitted herewith in triplicate is an Appeal Brief in this application with respect to the Notice of Appeal filed March 4, 2004. The required fee for submitting an appeal brief is estimated to be $330.

Applicant hereby petitions for an extension of time under 37 CFR 1.136 for 2 months. If an additional extension of time is required, please consider this a petition therefor. The required extension fee is estimated to be $420.

Please charge the required extension and appeal fees, estimated to be $750, to Novozymes North America, Inc., Deposit Account No. 50-1701. A duplicate of this sheet is enclosed.

Respectfully submitted,

Date: June 24, 2004

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APPEAL BRIEF

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Applicants hereby appeal from the final rejection of claims 47-58, all the claims pending in the present application.

I. REAL PARTY IN INTEREST

The name of the real party in interest in this appeal is Novozymes A/S.

II. RELATED APPEALS AND INTERFERENCES

There are no appeals or interferences relating to the instant application.

III. STATUS OF THE CLAIMS

Claims 47-58 remain pending in the application. Claims 1-46 have been canceled. All pending claims (copy attached) are included in this appeal.

IV. STATUS OF AMENDMENTS

The amendment filed under 37 C.F.R. § 1.116 on March 19, 2004 was considered, but has been stated as not overcoming the final rejection.

V. SUMMARY OF THE INVENTION

The claimed invention relates to methods for killing or inhibiting the growth of microorganisms with a composition comprising (a) a haloperoxidase at a concentration in the

range of 0.01-100 mg enzyme protein per liter, (b) a hydrogen peroxide source at a concentration in the range of 0.01-1000 mM, (c) a halide source at a concentration in the range of 0.01-1000 mM, and (d) a salt of NH_4^+ at a concentration in the range of 0.01-1000 mM. A salt of NH_4^+ is a salt of an ammonium ion, which consists of a nitrogen atom attached to four hydrogen atoms.

The specification demonstrates that there is a synergistic antimicrobial effect between a haloperoxidase and a salt of NH_4^+. Salts of NH_4^+ are not germicidal compounds, i.e., they do not have an anti-microbial effect.

In Example 3, Applicants have measured the antibacterial activity of a *Curvularia verruculosa* haloperoxidase using various ammonium halides. Specifically, approximately 10^6 cfu/ml of cells were incubated with the haloperoxidase and NH_4^+ salt for 15 minutes at 40°C. The results are provided in Table 1. Because the results are presented in log cfu/ml, the highest possible bactericidal activity is about 6. At a concentration of 0.25 and 0.5 mM, the use of NH_4I and NH_4Cl had a log cfu/ml of 6.2, which means that the combination of the NH_4^+ salt and haloperoxidase resulted in a total kill of cells. Moreover, at a concentration of 8 mM, the use of NH_4Br resulted in a total kill of cells. Even at a concentration of 4 mM, the use of NH_4Br resulted in a significant bactericidal activity. The results show that all of the ammonium salts tested and at all concentrations, a significant bactericidal activity was obtained.

VI. ISSUES

The outstanding issues are whether the claims are rendered obvious under 35 U.S.C. § 103 over Allen (U.S. Patent No. 5,389,369) taken with Winkler et al. (U.S. Patent No. 5,928,380) and Cantor et al. (U.S. Patent No. 3,539,520).

VII. GROUPING OF CLAIMS

For purposes of determining patentability, the following groups of claims are separately patentable and will be addressed separately:

Group I: claims 47, 48, 50, 51, 52, 53, 57, and 58;

Group II: claim 49;

Group III: claim 54;

Group IV: claim 55; and

Group V: claim 56.

VIII. ARGUMENTS

A. Claims 47-58 Are Not Rendered Obvious By The Cited References

1. The Legal Standard

It is well settled that the Patent and Trademark Office has the burden to establish a *prima facie* case of obviousness. *In re Rijckaert*, 28 U.S.P.Q.2d 1955, 1956 (Fed. Cir. 1993); *In re Fine*, 5 U.S.P.Q.2d 1596, 1598 (Fed. Cir. 1988). "In determining whether a case of *prima facie* obviousness exists, it is necessary to ascertain whether the prior art teachings would appear to be sufficient to one of ordinary skill in the art to suggest making the claimed substitution or other modification." *In re Lalu*, 223 U.S.P.Q. 1257, 1258 (Fed. Cir. 1984).

The standard for obviousness determinations is set forth in *In re Dow Chemical*, 5 U.S.P.Q.2d 1529, 1531 (Fed. Cir. 1988):

> The consistent criterion for determination of obviousness is whether the prior art would have suggested to one of ordinary skill in the art that [the claimed invention] should be carried out and would have a reasonable likelihood of success.... Both the suggestion and the expectation of success must be founded in the prior art not in the applicants' disclosure.

It is well settled that whether a modification is "obvious to try" is not the test of obviousness under 35 U.S.C. 103. See, e.g., *In re Geiger*, 2 U.S.P.Q.2d 1276, 1278 (Fed. Cir. 1987); *Jones v. Hardy*, 220 U.S.P.Q. 1021, 1026 (Fed. Cir. 1984).

> Slight reflection suggests ... that there is usually an element of 'obviousness to try' in any research endeavor, that it is not undertaken with complete blindness but rather with some semblance of a chance of success, and that patentability determinations based on that as the test would not only be contrary to statute but result in a marked deterioration of the entire patent system as an incentive to invest in those efforts and attempts which go by the name 'research.'

In re Tomlinson, 150 U.S.P.Q. 623, 626 (C.C.P.A. 1966).

The Federal Circuit has offered guidance as to the type of situations which fall within the meaning of "obvious to try."

> The admonition that 'obvious to try' is not the standard under § 103 has been directed mainly at two kinds of error. In some cases, what would have been 'obvious to try' would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful.... In others, what was 'obvious to try' was to explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it....

In re O'Farrell, 7 U.S.P.Q.2d 1673, 1681 (Fed. Cir. 1988).

Moreover, "[a]n invention is 'obvious to try' where the prior art gives either no indication of which parameters are critical or no direction as to which of many possible choices is likely to be successful." *Merck & Co. Inc. v. Biocraft Laboratories Inc.*, 10 U.S.P.Q.2d 1843, 1845 (Fed. Cir. 1989).

When the USPTO relies on a combination of prior art references to render a claimed invention obvious, the prior art references must contain within them a suggestion of the possibility of achieving the improvement of the claimed invention, such a suggestion being either express or implied. *In re Sernaker*, 217 U.S.P.Q. 1 (Fed. Cir. 1983). Obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching, suggestion or incentive supporting the combination. *Carella v. Starlight Archery*, 231 U.S.P.Q. 644 (Fed. Cir. 1986). References are non-analogous art when the references do not come from the same field of endeavor as the invention and are not usually pertinent to the solution of a problem solved by the invention. *In re Clay*, 23 U.S.P.Q.2d 1058 (Fed. Cir. 1992).

It is also impermissible to use the claims as a framework from which to pick and choose among individual references to recreate the claimed invention. *In re Fine*, 5 U.S.P.Q.2d 1596 (Fed. Cir. 1988). A reference or references must show or suggest the properties and results of the claimed invention, or suggest the claimed combination as a solution to a given problem, in order to successfully be relied upon for an obviousness rejection. *In re Wright*, 6 U.S.P.Q.2d 1959 (Fed. Cir. 1988).

It is also well established that an applicant can rebut a *prima facie* case of obviousness by demonstrating unexpectedly superior properties or advantages of the claimed invention as compared with the prior art.

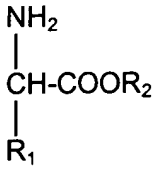
For example, if a process is *prima facie* obvious, the process can be unobvious within the meaning of 35 U.S.C. 103 by reason of an unsuggested increase in yield. *In re Von Schickh*, 150 U.S.P.Q. 300 (C.C.P.A. 1966). An applicant's allegation of unexpected results cannot be ignored merely because the claimed process is within the broad teachings of the prior art. *In re Costello*, 178 U.S.P.Q. 290 (C.C.P.A. 1973).

2. The Cited References

a. Allen - U.S. Patent No. 5,389,369

Allen discloses methods and compositions for killing or inhibiting the growth of yeast or sporular microorganisms comprising contacting the microorganisms with a haloperoxidase, a peroxide, a halide source and at least one antimicrobial activity enhancing agent. Suitable

antimicrobial activity enhancing agents are certain alpha-amino acids, preferably of the following formula



b. Winkler et al. - U.S. Patent No. 5,928,380

Winkler et al. disclose a method of treating undyed fabric, garment or yarn in an aqueous medium with a composition comprising an effective amount of a haloperoxidase, a halide source and a hydrogen peroxide source. The treated fabric is said to have improved shrink-resistance. Winkler et al. further disclose that the composition may comprise a buffer to maintain a suitable pH for the haloperoxidase (column 5, lines 47-55). Winkler et al. disclose a large number of buffers, one of which is ammonium carbonate. However, Winkler et al. do not contain any working examples of the combination of haloperoxidase and ammonium carbonate. Winkler et al. also do not teach or suggest the use of haloperoxidases for killing or inhibiting the growth of microorganisms.

c. Cantor et al. - U.S. Patent No. 3,539,520

Cantor et al. disclose detergent sanitizing compositions containing germicidal quaternary ammonium germicides in combination with a limited class of block polymer nonionic detergents (col. 2, lines 40-50). All of the germicidal compounds are quarternary ammonium compounds which contain four alkyl and/or aryl groups. However, Cantor et al. do not teach or suggest the use of salts of NH_4^+, as claimed herein.

3. Claims 47-58 Are Not Rendered Obvious By The Cited References

a. The Cited References Do Not Teach Or Suggest Applicants' Claimed Inventions

As discussed above, Allen discloses methods and compositions for killing or inhibiting the growth of yeast or sporular microorganisms using a haloperoxidase, a peroxide, a halide source and at least one antimicrobial activity enhancing agent which is an alpha-amino acid.

However, Allen does not teach or suggest that a salt of NH_4^+ is an enhancing agent. Furthermore, as stated above, salts of NH_4^+ are not germicidal compounds, i.e., they do not have

an antimicrobial effect. Thus, one of ordinary skill in the art would not have been motivated to replace an alpha-amino acid with a salt of NH_4^+.

Cantor et al. disclose detergent sanitizing compositions containing germicidal quaternary ammonium compounds in combination with a limited class of block polymer nonionic detergents. A quarternary ammonium compound is a nitrogen atom attached to four alkyl and/or aryl groups.

However, Cantor et al. do not disclose the use of a haloperoxidase and a salt of NH_4^+, as claimed herein. Moreover, since salts of NH_4^+ are not germicidal compounds, i.e., they do not have an antimicrobial effect, one of ordinary skill in the art would not have been motivated to replace the germicidal quarternary ammonium compound with a non-germicidal salt of NH_4^+.

Winkler et al. disclose a method of treating undyed fabric, garment or yarn in an aqueous medium with a composition comprising an effective amount of a haloperoxidase, a halide source and a hydrogen peroxide source to produce a fabric with improved shrink-resistance. Winkler et al. disclose that the composition may comprise a buffer to maintain a suitable pH for the haloperoxidase. One of a large number of buffers disclosed in Winkler et al. is ammonium carbonate.

However, Winkler et al. do not teach or suggest that ammonium carbonate enhances the anti-microbial activity of a haloperoxidase. Thus, one of ordinary skill in the art would not have been motivated to select ammonium carbonate from the large number of buffers in a method of killing or inhibiting the growth of microorganisms.

Moreover, since salts of NH_4^+ are not germicidal compounds and were not known to enhance the antimicrobial effect of haloperoxidases, one of ordinary skill in the art would not have been motivated to replace the alpha-amino acid enhancer of Allen or the germicidal ammonium compound of Cantor et al. with a salt of NH_4^+.

For the foregoing reasons, the cited references do not teach or suggest methods and compositions for killing or inhibiting the growth of microorganisms using a haloperoxidase and a salt of NH_4^+, as claimed herein. Applicants therefore submit that the Office has failed to establish a *prima facie* case of obviousness.

b. The Combination Of Haloperoxidase And Salt of NH_4^+ Has Surprising And Unexpected Properties

The specification demonstrates that the combination of a haloperoxidase and a salt of NH_4^+ results in an increased antibacterial activity. These results are surprising and unexpected.

In Example 3, Applicants have measured the antibacterial activity of a *Curvularia verruculosa* haloperoxidase using various ammonium halides and potassium and sodium salts.

Specifically, approximately 10^6 cfu/ml of cells were incubated with the haloperoxidase and NH_4^+ salt for 15 minutes at 40°C. The results are provided in Table 1. At a concentration of 0.25 and 0.5 mM, the use of NH_4I and NH_4Cl had a log cfu/ml of 6.2, which means that the combination of the NH_4^+ salt and haloperoxidase resulted in a total kill of cells. Moreover, at a concentration of 8 mM, the use of NH_4Br resulted in a total kill of cells. Even at a concentration of 4 mM, the use of NH_4Br resulted in a significant bactericidal activity. The results show that a significant bactericidal activity was obtained for all of the ammonium salts tested and at all concentrations. On the other hand, the combination of the haloperoxidase and potassium and sodium salts have a lower anti-microbial effect.

In response, the Office stated the following:

> While the reference admittedly differs from the claimed invention in that the amino acids are not ammonium salts, applicant has only demonstrated that the use of ammonium salts has an unexpected effect whenever the concentration of the ammonium ion [is] 0.25 to 50 mM using *Curvularia* haloperoxidase using *S. epidermidis*. There is no evidence of record to demonstrate unexpected effects at ammonium concentrations lower than 0.25 mM or higher than 50 mM. Therefore the scope of the showing is not commensurate in scope with the scope of the claims.

This is respectfully traversed.

As discussed above, haloperoxidases are known to be antimicrobial agents. Thus, although the examples tested the antimicrobial effect against *S. epidermidis*, one of ordinary skill in the art would expect similar results with other haloperoxidases and other microorganisms.

Moreover, the results show that a significant bactericidal activity was obtained with all of the ammonium salts tested and at all concentrations. Specifically, at a concentration of 0.25 and 0.5 mM of NH_4I and NH_4Cl and at a concentration of 8 mM of NH_4Br, a total kill of cells was achieved. One skilled in the art would expect that if a larger amount of the ammonium salts is used, a total kill of cells would be obtained. Even at a concentration of 4 mM, the use of NH_4Br resulted in a significant bactericidal activity. Based on these results, one of ordinary skill in the art would expect that salts of NH_4^+ would have a greater bactericidal activity than other salts, when tested in the same amount.

In summary, there is no evidence that the antimicrobial effect is dependent on the amount of ammonium salt used.

c. Claims 49, 54, 55 and 56 Are Separately Patentable

The cited references also do not teach or suggest the methods of claims 49, 54, 55 and 56. In particular, none of the cited references teach or suggest (1) vanadium haloperoxidase

(claim 49), (2) the use of diammonium sulphate, ammonium chloride, ammonium bromide, or ammonium iodide as enhancers of the anti-microbial activity of a haloperoxidase (claim 54), the use of sodium chloride as the halide source and diammonium sulphate as the ammonium salt (claim 55), and the use of the same halide source and salt of NH_4^+ (claim 56).

Applicants therefore request that if the Board affirms the 103 rejection of claims 47, 48, 50, 51, 52, 53, 57, and 58, that it reverse the 103 rejection of claims 49, 54, 55 and 56.

IX. CONCLUSION

For the foregoing reasons, Applicants submit that claims 47-58 are not rendered obvious by the cited references. Accordingly, the final rejection of the claims should be reversed.

Respectfully submitted,

Date: June 24, 2004

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APPENDIX

Copy of Claims Involved in the Appeal

47. A method of killing or inhibiting the growth of microorganisms, comprising contacting the microorganisms with a composition comprising (a) a haloperoxidase at a concentration in the range of 0.01-100 mg enzyme protein per liter, (b) a hydrogen peroxide source at a concentration in the range of 0.01-1000 mM, (c) a halide source at a concentration in the range of 0.01-1000 mM, and (d) a salt of NH_4^+ at a concentration in the range of 0.01-1000 mM.

48. The method of claim 47, wherein the concentration of the haloperoxidase is in the range of 0.05-50 mg enzyme protein per liter, the concentration of the halide source is 0.05-500 mM, and the concentration of the salt of NH_4^+ is 0.05-500 mM.

49. The method of claim 47, wherein the haloperoxidase is a vanadium haloperoxidase.

50. The method of claim 47, wherein the haloperoxidase is a chloride peroxidase or a bromide peroxidase.

51. The method of claim 47, wherein the source of hydrogen peroxide is hydrogen peroxide, a hydrogen peroxide precursor, a hydrogen peroxide generating enzyme system, or a peroxycarboxylic acid or a salt thereof.

52. The method of claim 47, wherein the halide source is a halide salt.

53. The method of claim 52, wherein the halide source is potassium bromide, potassium chloride, potassium iodide, sodium bromide, sodium chloride, or sodium iodide.

54. The method of claim 47, wherein the salt of NH_4^+ is diammonium sulphate, ammonium chloride, ammonium bromide, or ammonium iodide.

55. The method of claim 47, wherein the halide source is sodium chloride and the ammonium salt is diammonium sulphate.

56. The method of claim 47, wherein the halide source and the salt of NH_4^+ are the same.

57. The method of claim 47, wherein said composition is an aqueous composition.

58. The method of claim 47, wherein the composition is a granulate.